



**ASPR**

# Zika Virus Vaccine Efforts

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# ASPR's Mission



# Establishment of BARDA



**PBS – 2004**

- \$5.6B advanced appropriation to develop Medical Counter Measures (MCMs) against Chemical, Biological, Radiation, and Nuclear (CBRN) threats



**PAHPA – 2006**

- Established the ASPR and BARDA
- BARDA threat space: CBRN, Pandemic Influenza (PI), and Emerging Infectious Diseases
- Authority to invest in Advanced Research and Development (ARD) and Emergency Use Authorizations



**PAHPRA – 2013**

- New, yearly funds for ARD: \$415M
- Reauthorization of Project BioShield (PBS): \$2.8B
- PI was not included
- Historic investments \$350-\$400M annually with supplemental

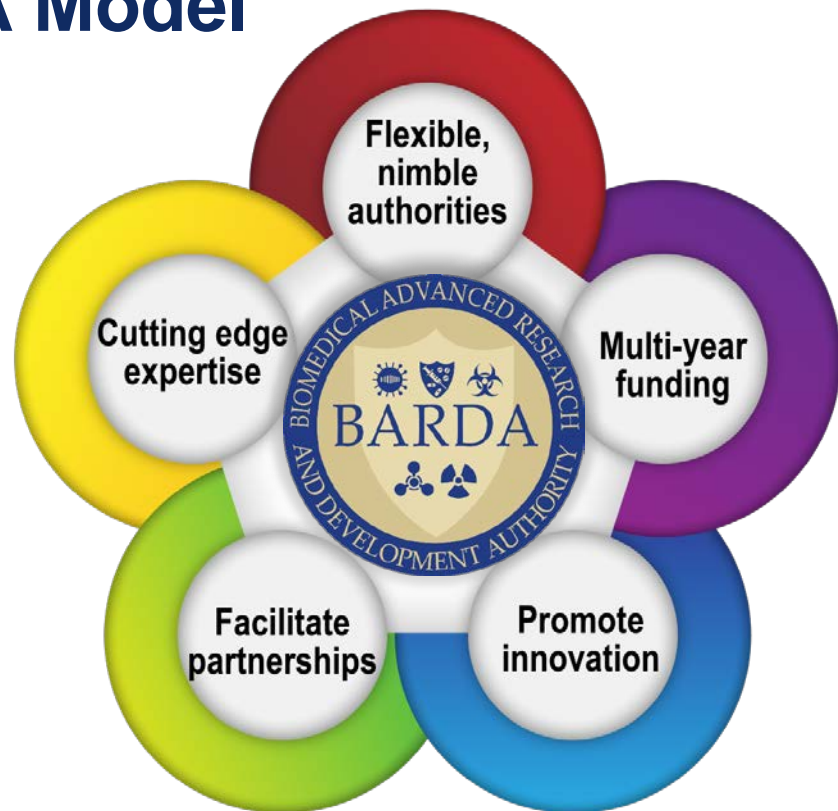


**21<sup>st</sup> Century Cures Act – 2016**

- Restore BARDA Contracting
- Medical Countermeasures Innovation Partnership (MCIP) Program

# The BARDA Model

- BARDA develops and makes available medical countermeasures (**MCMs**) by forming unique public-private partnerships with industry partners



# BARDA Zika Priorities

## 1. Detect Zika Infection

- Support advanced development of rapid serological diagnostics, including point of care, for the detection of antibodies in persons previously infection with Zika virus

## 2. Prevent Zika Infection

- NIH/DOD/BARDA collaboration for USG-developed, manufactured, and evaluate Zika virus vaccine
- NIH and BARDA to support private sector development of vaccine through federal funding opportunities
- HHS to support international collaborations, including vaccine production at the Butantan Institute in Brazil

## 3. Secure and protect blood supply

- Support advanced development of high throughput molecular diagnostics for screening blood supply
- Support late stage pathogen reduction systems



# Prevent Zika Virus Infection

- Vaccine for other flaviviruses have been developed and used for over 70 years
- Active development programs for Dengue and West Nile vaccines have been ongoing for over 30 years, explored a variety of vaccine platforms to develop vaccines for these flaviviruses
- Experiences gained and vaccine platforms developed for other flaviviruses are being leveraged for ZIKV vaccine development

# WRAIR ZIPV

## Walter Reed Army Institute of Research

- Zika Purified Inactivated Vaccine (ZPIV)
  - Based on JEV vaccine technology
  - Formalin inactivated, alum adjuvanted virus
- Phase 1 clinical trials
  - Naïve vs. YF or JE vaccinated
  - Dose optimization
  - Accelerated schedule
  - Natural flavivirus immunity
- Successful proof of concept and tech transfer to Sanofi Pasteur



# WRAIR

Walter Reed Army  
Institute of Research

Soldier Health • World Health

# Sanofi Pasteur ZPIV

## Halted vaccine development

- Corporate decision

## Case Definition Study

2400 subjected enrolled, (400 Puerto Rico, [1 site], 700 Colombia [1], 500 Honduras [1] and 800 Mexico [2])

- Sample and data analysis is on-going

**sanofi pasteur**

The vaccines division of sanofi-aventis Group



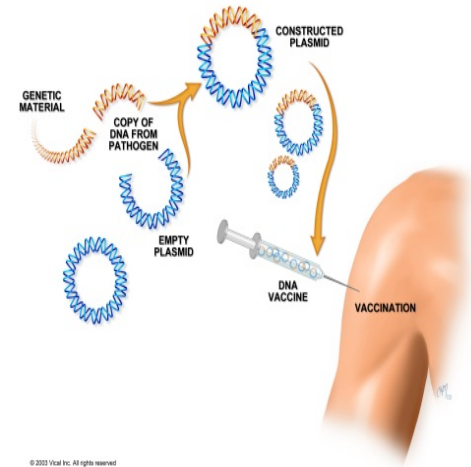
# Takeda Zika Virus Vaccine, ZIPV

- Developing a whole inactivated Zika virus vaccine to be administered with alum adjuvant
- Initiated Phase 1 Clinical Trial of Zika Vaccine Candidate – November 2017
  - Safety and immunogenicity in 240 subjects
  - 3 doses (2, 5, 10 ug) placebo controlled
  - Ages 18-49
  - Sites in the continental U.S. and Puerto Rico
  - Vaccinating flavivirus naïve and primed



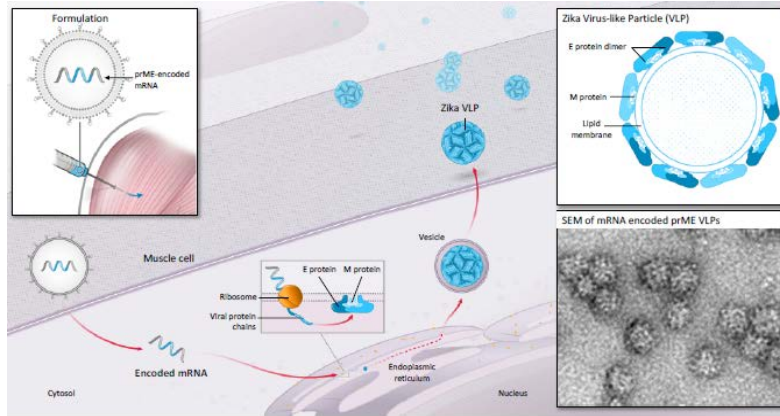
# VRC DNA Vaccine Milestones

- Phase 1 Clinical Trials – 2 candidates: VRC 5288 and VRC 5283
  - Interim data reported in Lancet, Dec. 2017 (Gaudinski et al)
  - Zika neutralizing antibodies developed in 100% of subjects
- Phase 2a/2b Clinical Trial – VRC 5283
  - Part A: Dose Escalation and Injection Number Study
    - Enrollment complete
    - Immunogenicity evaluation ongoing
  - Part B: Efficacy Study
    - Regimen selected May 2017
    - Enrollment initiated July 2017
    - Study is on-going
- Industry partner identified for commercialization



# Moderna mRNA Vaccine

- Vaccine Delivery Approach



- New construct
  - 10ug dose superior to 200ug

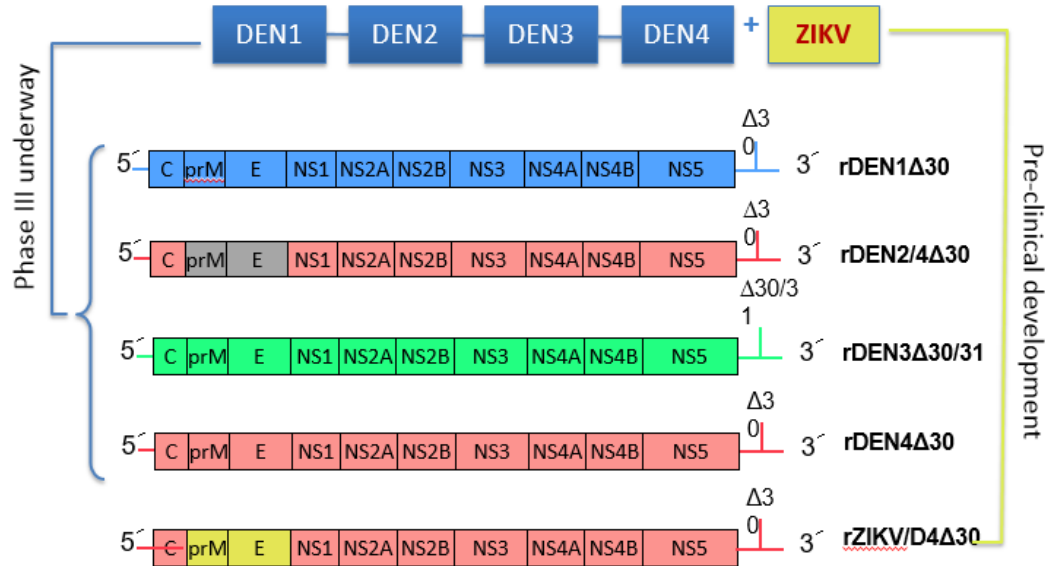
	mRNA-1325	mRNA-1706	mRNA-1893
Antigen	Zika prME	Zika prME	Zika prME
Signal Peptide	IgE	IgE	New
Form	In-Licensed	V1GL	V1GL
GLP Tox	✓	✓	TBD

Transitioning

- Rapid, multi-product platform potential

**moderna™**  
messenger therapeutics

# Pentavalent DENV + ZIKV



Courtesy: S. Whitehead, LVD/NIAID

#	Deliverable	Timeline (CY)	DONE? ✓
1	Virus construction, seed virus generation, pre-clinical evaluation	Q2 2017	✓
2	Manufacturing of Phase 1 and 2 CTM's at Charles River Laboratories; Release testing	June – Nov 2017	✓
3	IND submission	Feb 2018	Initiated
4	Phase 1 - Monovalent	March 2018	
5	Phase 2 - Pentavalent	May 2018	
6	Phase 2a – Butantan Institute Bridging, Monovalent, Pentavalent	Pending Q4 2018	
7	Phase 2b – Butantan Institute	Pending 2019	

# USG Task Orders Supporting Zika Vaccine Development

## GENERATION OF CHALLENGE VIRUS (PRVABC59)



### CoA

PFU/ml  
Genomes/ml  
Endotoxin  
Mycoplasma  
Sequence  
Documented passage history

## NATURAL HISTORY STUDY

Dose Ranging

### Re-Challenge

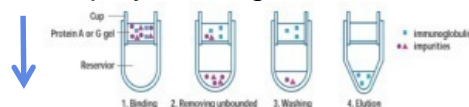
- Viral loads
- Immune response
- Correlates of protection

### Challenge

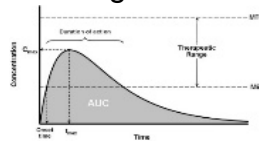
- Viral loads
- Tissue distribution
- Immune response

## PASSIVE TRANSFER/CHALLENGE MODEL

Purify and characterize polyclonal IgG



IgG Pharmacokinetic profile



Passive transfer/challenge study in mice



## Benefits to MFRs

- Protocols
- Reagents
- Qualified assays

**PRECLINICAL DATA PACKAGE**

TO 19

Assays

PFU RT-qPCR PRNT MN RVP  
Development Qualification

BIO-AMT-1004

BIO-AMT-1008

NIAID

Preclinical testing in NHP model

TO 26

## PRESS RELEASE

Emergent BioSolutions and Valneva Initiate Phase 1 Clinical Study to Evaluate Vaccine Candidate Against Zika Virus

Gaithersburg, Md. and LYON, France, Feb 26, 2018 (GLOBE NEWSWIRE) -- Emergent BioSolutions Inc. (NYSE:[EBS](#)) and Valneva SE (Euronext Paris:VLA) today announced the initiation of a Phase 1 clinical trial in the U.S. to evaluate the safety and immunogenicity of VLA1601, their vaccine candidate against Zika virus.

The Phase 1 clinical trial is a randomized, observer-blinded, placebo-controlled, single center study. This study, in approximately 65 healthy adults, will investigate two dose levels of VLA1601 when administered using two different vaccination schedules. Initial data from the trial are expected to be available in late 2018 or early 2019.

# Inovio Pharmaceuticals DNA Vaccine



The NEW ENGLAND  
JOURNAL of MEDICINE

October 4, 2017



## **Safety and Immunogenicity of an Anti-Zika Virus DNA Vaccine — Preliminary Report. Pablo Tebas *et al.***

- DNA plasmid vaccine expressing Zika prM-E
- Two groups of 20 received 1mg or 2 mg ID at 0, 4, 12 weeks w/electroporation
- No SAEs reported
- Anti-Zika antibodies detected in 100% in both groups
- Zika neutralizing antibodies developed in 62% of subjects
- Passive transfer of human vaccinee serum protected in a lethal mouse model

# Themis Measles Recombinant Vector



## PRESS RELEASE

Zika Virus: Themis Bioscience Initiates Worldwide First Study With Live Attenuated Recombinant Vaccine

Vienna, Austria, 11-Apr-2017 – A promising vaccine for the Zika virus is now being tested by **Themis Bioscience GmbH**, a specialized biotech company developing prophylactic vaccines against emerging tropical infectious diseases. After recent progress with the development of a Chikungunya vaccine the company succeeded in swiftly adapting their proprietary vaccine technology for their Zika vaccine program.

This program is based on a live attenuated recombinant vaccine that promises a fast and effective immune response.



# Zika Virus Vaccines Landscape – June 2018

